U.S. Application Serial No. 09/672,865

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re the Application of:	Group Art Unit: 1632
GELFAND et al.	Examiner: Li, Quan J.
Serial No.: 09/672,865	
Filed: September 28, 2000	DECLARATION OF ERWIN W. GELFAND (Under 37 CFR 1.132)
Atty. File No.: 2879-68	
For: "REGULATION OF γδ T CELLS TO REGULATE AIRWAY HYPERRESPONSIVENESS"	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Erwin W. Gelfand, declare as follows:

1. I am a co-inventor of the above-referenced patent application and am familiar with the application. I am a skilled artisan in the fields of immunology and disorders of the airways.

2. This Declaration is being submitted in conjunction with an Amendment and Response to an Office Action having a mailing date of April 11, 2003.

3. The following discussion is provided in response to the Examiner's rejection of Claims 1, 2, 4, 14, 17-19, 22-33, and 36-38 under 35 U.S.C. § 112, first paragraph. Specifically, the following discussion and attached figures demonstrate that administration of tumor necrosis factor-α (TNF-α) inhibits airway hyperresponsiveness in sensitized and challenged mice, and that this effect is mediated via an effect on the activity of γδ T cells. The data also show that administration of TNF-α reduces airway hyperresponsiveness independently of cellular inflammation in the lung.

More specifically, Figure A shows the study protocol for the experiments described herein. Briefly, using the protocols as described in the Examples of the above-identified application for the experimental model of airway hyperresponsiveness, mice were sensitized and challenged with ovalbumin, and airway responsiveness was assessed as a change in airway function after challenge with aerosolized methacholine (MCh). Also as described in the present application, maximum values

of R_L, and minimum values of C were used to express changes in murine airway function. Three groups of mice were depleted of γδ T cells by administration of monoclonal antibody against TCR-δ as described in the application at days 24 and 25 after the initial sensitization to ovalbumin. Two of the groups of γδ-depleted mice, and two groups of mice with intact γδ T cells were administered either 5ng or 500ng of TNF-α, or with PBS as a control, intranasally before the first nebulized ovalbumin challenge at day 28 and between the second and third ovalbumin challenges at days 29 and 30. 48 hours later, determination of airway responsiveness and inflammation was assessed using aerosolized methacholine (MCh) and examination of BAL fluid, respectively, as described in detail in the application.

Figure B shows that administration of 500 ng of TNF-α reduced airway hyperresponsiveness as compared to controls in both the larger airways, as assessed by airway resistance (R_L) and the smaller airways, as demonstrated by changes in dynamic lung compliance. In mice lacking γδ T cells, the effect of TNF-α was abolished, indicating that the effect of the TNF-α treatment relies on the presence of γδ T cells, as already set forth in the above-identified application.

Figure C shows the BAL fluid cell composition for total cells, macrophages, lymphocytes, neutrophils and eosinophils. These results show that inflammation as measured by the numbers of cells in the BAL fluid did not significantly change with treatment. Therefore, the effect of the TNF-α treatment is not associated with inflammation in the lung.

Therefore, these data show that administration of TNF-α reduces airway hyperresponsiveness, that this effect is associated with γδ T cells, and that the effect is not associated with inflammation.

4. I hereby declare that all statements made herein of my own are true and that all statements made on information and belief are believed to be true; and further that the statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the subject application or any patent issuing therefrom.

Date: 10.10.03 By: _____

Erwin W. Gelfand